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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,241	06/26/2000	NORIAKI HATTORI	193582US0PCT	3276

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 12/14/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/581,241

Applicant(s)

HATTORI ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 June 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

This application is a 371 of PCT/JP98/05864.

The preliminary amendment filed October 29, 2001 amending the specification to replace the original Sequence Listing with a substitute Sequence Listing has been entered.

Claims 1-13 are pending.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The references cited in the Search Report filed June 26, 2000 have been considered, but will not be listed on any patent resulting from this application with exception of the references cited on PTO-892 attached hereto because they were not provided on a separate list in compliance with 37 CFR 1.98(a)(1). In order to have the references printed on such resulting patent, a separate listing, preferably on a PTO-1449 form, must be filed within the set period for reply to this Office action.

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Drawings

The drawings filed concurrently with the application have been approved by Draftsperson.

Specification

The disclosure is objected to because subtitles are given in brackets or parenthesis throughout the text, for example, on pages 5, 7, 10, 14, etc. rendering the text confusing. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to a luciferase of any structure and properties having resistance to a surfactant. While referring to the luciferase from *Luciola lateralis* (HEIKE) or *Luciola cruciata* (GENJI), claims 2 and 3 do not impart any limitation on the

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structure except for the mutation at position 490. Claims 4 and 5 recite a polypeptide comprising additions, deletions, or substitutions in SEQ ID NOs:4 or 6. Since number of possible mutations is not limited, this amounts to any structure that is not necessarily homologous to SEQ ID NOs:4 or 6. Claims 6-13 depend from claim 1-5. Thus, the claims are drawn to an enormous genus of a luciferase both naturally occurring and man made or mutated luciferase having resistance to a surfactant.

Applicants disclose two mutants of *L. lateralis* luciferase having resistance to a surfactant having sequences of SEQ ID NOs: 4 and 6 that comprise mutation E490K. (These two sequences differ by the mutation at 217 wherein SEQ ID NO:4 has A217L and SEQ ID NO:6 has A217I). Therefore, a representative number of a luciferase mutated at 490 is two. Moreover, the specification fails to describe any other representative species including luciferases from other sources by any identifying characteristics or properties other than the "functionality" of being resistant to surfactant and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

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Claims 1 and 4-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *Luciola lateralis* or *Luciola cruciata* luciferases mutated at position 490 resistant to a surfactant (SEQ ID NO:4 or SEQ ID NO:6), does not reasonably provide enablement for any luciferase having unknown homology thereto with this mutation or to any luciferase possessing resistance to a surfactant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Claim 1 is directed to a luciferase of any structure and properties having resistance to a surfactant. Claims 4-13 are so broad as to encompass any luciferase with unknown possible low homology to the luciferase of *Luciola lateralis* in which the amino acid corresponding to residue 490 is substituted, polynucleotides encoding for such a luciferase and methods of use of such luciferases. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of luciferase enzymes and genes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to

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modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and amino acid sequence of a single luciferase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any luciferase with even low homology to the luciferase of *Luciola lateralis* in which the amino acid corresponding to residue 490 of *Luciola lateralis* luciferase is mutated or polynucleotides encoding therefor because the specification does not establish: (A) regions of the protein structure which may be modified without effecting luciferase activity; (B) the general tolerance of luciferases to modification and extent of such tolerance; © a rational and predictable scheme for modifying any luciferase residues with an expectation of obtaining the desired biological function; and (D) the

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specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any luciferase with no or low homology to the luciferase of *Luciola lateralis* in which the amino acid corresponding to residue 490 is mutated. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of luciferases and genes therefor having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 1-13 are indefinite for their recitation of the 490 amino acid position without indicating a sequence identifier of the sequence where said position is located. It is unclear which residue is implied because different luciferases have different sequences. References to SEQ ID NOs of respective wild-type luciferases would obviate this rejection.

Claim 10 is confusing because some words on lines 1 and 2 are redundant.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1 and 10-13 is rejected under 35 U.S.C. 102(b) as being anticipated by

Simpson et al.

Simpson et al. teach *Photinus pyralis* luciferase that is resistant to non-ionic and zwitterionic surfactants (page 100, Table 1; page 105, 2nd column).

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Claims 1 and 4-13 is rejected under 35 U.S.C. 102(b) as being anticipated by Tatsumi et al.

Tatsumi et al. teach wild type *Luciola lateralis* luciferase and its cloning. This luciferase has activity in an assay for measuring ATP in the presence of a surfactant (see, for example, the specification Tables 1 and 2). Claim 1 is limited by neither degree of resistance nor the nature of a surfactant. Therefore, the luciferase of Tatsumi et al. anticipates claims 1 and 6-13. Claims 4 and 5 are anticipated because, as discussed above, there is no limitations on the structure of the claimed luciferases.

Claims 1-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Hirokawa et al.

The applied reference has a common assignee and one common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Hirokawa et al. (US Patent 6,074,859) teaches SEQ ID NO: 14 that has 99.8% identity to SEQ ID NO:4 and 99.7% identity to SEQ ID NO: 6 of the instant invention.

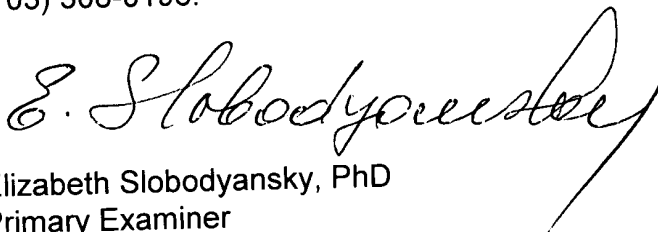
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SEQ ID NO:4 of the instant invention differs from SEQ ID NO:14 disclosed in the Hirokawa et al. patent only by substitution T219I. SEQ ID NO:6 of the instant invention differs from said sequence by two substitutions L217I and T219I. Both Hirokawa et al. sequences have E490K substitution. Hirokawa et al. teach methods for measuring ATP using luciferase (Example 5).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.



Elizabeth Slobodyansky, PhD
Primary Examiner

December 11, 2001